SECTION - I

INTRODUCTION

Medicinal chemistry includes synthesis of novel medicinal compounds, the study of already existing drugs, of their biological properties and their structure-activity relationships. It explains the design and production of compounds that can be used for the prevention, treatment or cure of human and animal diseases. During the early stages of medicinal chemistry development, scientists were primarily concerned with the isolation of medicinal agents found in plants. Today, scientists in this field are also equally concerned with the creation of new synthetic compounds as drugs. The focus on development of new synthetic drug compounds has resulted in the incorporation of many other disciplines, such as biochemistry and molecular biology into medicinal chemistry. These areas include biology, computer-aided drug design, X-ray crystallography, metabolism and pharmacokinetics [1-4].

The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. Heterocycles containing nitrogen are most abundant in nature than those containing oxygen or sulphur. Heterocyclic compounds are of particular interest in medicinal chemistry and this has catalyzed the discovery and development of many new heterocyclic chemistry and methods. A large number of heterocyclic compounds are essential to life. Many heterocyclic compounds are biosynthesized by plants and animals and are biologically active. Over millions of years, these organisms have been under intense evolutionary pressure and their metabolites may be used to advantage for example, as colouring agents to attract mates or pollinating insects [5-8].

Schiff bases form an important group of compounds in synthetic chemistry due to their useful physical and chemical properties and large number of reactions. Schiff bases are also used widely in pharmaceutical industry and have interesting pharmacological activities [9]. Schiff base (or azomethine) is a functional group that contains a carbon nitrogen double bond with the nitrogen atom connected to an aryl or alkyl group but not hydrogen. Schiff bases are usually synthesized from the condensation of primary amines and active carbonyl group [10].

The condensation of primary amines with carbonyl compounds was first reported by Schiff [11], and the condensation products are often referred to as Schiff bases. This condensation reaction, along with the chemical and physical properties of Schiff bases have been reviewed [12]. Schiff bases are also known as anils, imines, or azo methines.

A large number of Schiff bases have been found to exhibit pharmacological activity like antibacterial, antifungal**,** tuberculostatic [13], antimicrobial, anticancer, anti-inflammatory [14], cardiovascular agents and anti HIV [15].

Benzothiazoles are well known for their cytotoxic activity. Apart from this, they have shown variety of potent biological activities as reflected in the literature. Benzothiazoles when combined with other aromatic and hetero-aromatics have shown a great diversity in their biological properties[16-21]. Benzothiazole derivatives find use in various branches of chemical research e.g. in polymer chemistry [22], dyes [23], drugs [24-25] etc.

A broad spectrum of pharmacological properties has been demonstrated by the benzothiazole nucleus. Benzothiazole derivatives have attracted a great deal of interest due to their anti-inflammatory, antitumor, antiglutamate, anticancer activity, antiasthmatic, breast cancer, photosynthesis-inhibiting activity etc [26-27]

The extensive use of antibiotics has led to the appearance of multi-drug resistant microbial pathogens [28, 29] The design of novel chemotherapeutic agents is particularly beneficial due to their dissimilar mode of action which can avoid cross resistance to known drugs. 4-Thiazolidinones have received considerable attention due to their wide range of biological activities. 4-Thiazolidinone derivatives are known to possess antimicrobial [30-34], analgesic [35], anti-inflammatory [36, 37], anti-HIV activity [38], cytotoxic activity [39], anticonvulsant [40], antiarrhythmic [41-42] etc

SECTION - II

EXPREMENTAL

Series-I: Synthesis of 4,4'- methylene bis *N*- substituted benzylidine-2-methyl aniline

The title compounds were synthesized by reacting o- toluidine with formaldehyde in acidic medium and then condensed with various aromatic aldehyde in methanol in presence of acetic acid.

Series-II: Synthesis of 4,4'- methylene bis *N*- substituted benzylidine-3-nitro aniline

The title compounds were synthesized by reacting 3-nitro aniline with formaldehyde in acidic medium and then condensed with various aromatic aldehyde in methanol in presence of acetic acid.

Series-III: Synthesis of 3,3'-(4,4'-methylenebis(2-methyl-4,1-phenylene))bis(2-(2-substituted phenyl thiazolidinone 4-one)

The title compounds were synthesized by refluxing 4,4'- methylene bis *N*- Substituted benzylidine-2-methyl aniline with 1,4- dioxane and thio glycolic acid in presence of anhydrous $ZnCl_2$ in acidic medium.

Series-IV: Synthesis of 3,3'-(4,4'-methylenebis(3-nitro-4,1-phenylene))bis(2-(2-substituted phenyl thiazolidinone 4-one)

The title compounds were synthesized by refluxing 4,4'- methylene bis *N*- Substituted benzylidine-3-nitro aniline with 1,4- dioxane and thio glycolic acid in presence of anhydrous $ZnCl_2$ in acidic medium.

Series-V: Synthesis of 6,6'- methylene bis (*N*- Substituted benzylidine-4-methyl benzo[*d*]thiazole-2-amine)

The title compounds were obtained by the cyclisation of 44'- methylene bis 2- methyl aniline with bromine, potassium thiocyanate, in acidic medium and then condensed with various aromatic aldehyde in methanol in presence of acetic acid.

Series-VI: Synthesis of 6,6'- methylene bis (*N*- Substituted benzylidine-5-nitro benzo[*d*]thiazole-2-amine)

The title compounds were obtained by the cyclisation of 44'- methylene bis 3- nitro aniline with bromine, potassium thiocyanate, in acidic medium and then condensed with various aromatic aldehyde in methanol in presence of acetic acid.

Series-VII: Synthesis of 3,3'- (6,6'-methylenebis(4-methylbenzo[*d*]thiazole-6,2-diyl))bis(2-phenylthiazolidin-4-one)

The title compound were synthesized by refluxing 6,6'- methylene bis (*N*- Substituted benzylidine-4-methyl benzo[*d*]thiazole-2-amine) with 1,4- dioxane and thio glycolic acid in presence of anhydrous $ZnCl_2$ in acidic medium.

Series-VIII: Synthesis of 3,3'-(6,6'-methylenebis(5-nitrolbenzo[*d*]thiazole-6,2-diyl))bis(2-phenylthiazolidin-4-one)

The title compound were synthesized by refluxing 6,6'- methylene bis (*N*- Substituted benzylidine-5-nitro benzo[*d*]thiazole-2-amine) with 1,4- dioxane and thio glycolic acid in presence of anhydrous $ZnCl_2$ in acidic medium.

SECTION - III

CHARACTERIZATION

All the heterocyclic compounds were characterized by thin layer chromatography, elemental analysis, infrared spectra and some of the representative by PMR spectra.

SECTION – IV

BIOLOGICAL EVALUATION

All the synthesized compounds have been evaluated for their *in vitro* biological assay like antimicrobial activity towards gram positive and gram negative microbial strains. The biological activities of the synthesized compounds have been compared with standard drugs.

REFERENCES:

1. Sainsbury M., Heterocyclic Chemistry, *RSC Publishing*, 8 **(2001)**.

2. Sharma A. and Shah M. K., *Chem Sci Trans.*, 2(3) **(2013)** 871-876.

3. Alajarin M.,Vidal A., Tovar F., Jones P. G. and Boustita B., *Arkovic,* 9 **(2005)** 39.

4. Evindar G. and Batey R. A., *J. Org. Chem.,* 71 **(2006)** 1802.

5. Downer N. K. and Jackson Y. A., *Org. Biomol. Chem.*, 2 **(2004)** 3039.

6. Reddy R.S., and Sudhakar D., *Scholars Research Library*, 6(1) **(2014)** 111-114.

7. Cojocariu C. and Rochon P., *J . Mater. Chem.*, 14 **(2004)** 2909.

8. Chen L., Cui Y., Qian G. and Wang M., *Dyes Pigments*, 73 **(2007)** 338.

9. Vicini P., Geronikaki A., Anastasia K., Incerti M., zani F., *Bioorg. Med. Chem*. 14 **(2006)** 3859-3864.

10. Mehta P.D., Sengar N.P., Subrahmanyam E.V., Satyanarayana D., *Indian J.Pharm. Sci*. 68 **(2006)** 103-106.

11. Altintas H., Ates O., Birteksoz S., Otuk G., Uzun M., Satana D., *Turk. J. chem.* **29 (2005)** 425-435.

12. Choudhari B. P. and Mulwad V. V., *Indian J Chem. ,* 44B **(2005)** 1074.

13. Kucukguzel G., Kocatepe A., Clercg E. D., Sahin F., and Gulluce M., *Eur. J. Med. Chem* 41 **(2006)** 353-359.

14. Mujeebur V. P. and Lemiere G., *Eur. J. Med. Chem*., 40 **(2005)** 173.

15. Amr A., Sabrry N.M., Abdalla M.M., Abdel B.F., *Eur. J. Med. Chem*. **(2008)** 1-11.

16. Mehta P., Dawedra P., Goswami V., Joshi H.S., *International Letters of Chemistry, Physics and Astronomy*, 11(1) **(2014)** 1-8.

17. Kini S., Swain S., Gandhi A., *Ind. J. Pharm. Sci.*, 69 **(2007)** 46.

18. Mustapha M., Thorat B.R., Sawant S., Atram R.G., *J. Chem. Pharm. Res*., 3(4) **(2011)** 5-9.

19. Sinha D., Tiwari A.K., Singh S., Shukla G., Mishra P., Chandra H. and Mishra A.K., *Eur J Med Chem.,* **(2007)** 1-6.

20. Schiff H., *Annls. Chem***.,** 31 **(1864)** 118.

21. Catalano A., Carocci A., Defrenza I., Muraglia M., Carrieri A.,Rosato A., Corbo F., *Eur. J. Med. Chem*, 64 **(2013)** 357-364.

22. Bag B., Das D., and Sinha C., *Ind. J. Chem*, 39B **(2000)** 787.

23. Sodhi S., Singh N., Kumar A., Lozach O. and Meijer L., *Bioorg. Med. Chem.* 14 **(2006)** 3758.

24. Al-Abed Y., Dubrovsky L., Ruzsicska B., Seepersaud M. and Bukrinsky M., *Bioorg. Med. Chem. Lett.*, 12 **(2002)** 3117.

25. Anderson, Terwisscha A. C., Valegard K., Cell; *Mol. Life Sci*.58 **(2001)** 1897.

26. Frere J.M., *Mol. Microbiol*. 16 **(1995)** 385.

27. Bondock S., Khalifa W., Fadda A., *Eur. J. Med. Chem*. 42 **(2007)** 948-95.

28. Asundaria S., Patel K., *Synth. Commun.*, 40 **(2010)** 1899.

29. Mohomad A. and Faizal A., *Ind. J. Hetero. Chem.*, 14 **(2004)** 119.

30. Andreani A., Granaiola M., Leoni A., Locatelli A., Morigi R., Rambadli M., Giorgi G. and Salvini L., *Arkivok* 11 **(2002)** 32.

31. Chawla P., Singh R., Saraf S. K., *Med Chem Res* 21 **(2012)** 2064–2071.

32. Srivatava S., Srivastava G. and Srivastava S., *Ind. J. Chem.,* 41B **(2002)** 1937.

33. Kakade P. K., *J. Chem. Pharm. Res.*, 5(2) **(2013)** 299- 304.

34. Chua M., Shi D., Wrigley S., Bradshaw T., Hutchinson I., Shaw P., Barrett D., Stanley L. and Stevens M., *J. Med. Chem.*, 42 **(1999)** 381.

35. Podila N., Pattanaik P. and Bhukya R., *Int J Pharma Sci*., 3(2) **(2013)**170-174.

36. Lokapure S. G., Shivakumar B. and Kalyane N. V., *Scholars Research Library*, 5(3) **(2013)** 21-26.

37. Frere S., Thiery V. T. and Besson, *Synthetic Communication*, 33 **(2003)** 3794.

38. Shaikh Z. K., Hisamoddin, Sanchaity P., Sharma P., Patel N., Patel U., *Int J Pharma Sci*., 5(1) **(2014)** 207.

39. Patai S., The Chemistry of carbon-nitrogen double bond, *Interscience Publishers Inc*, Newyork, **(1970).**

40. Rudrapal M., and Biplab De, *International Research Journal of Pure & Applied* Chemistry, 3(3) **(2013)** 232-249.

41. Mehta P., Dawedra P., Goswami V., Joshi H. S. *International Letters of Chemistry, Physics and Astronomy*, 11(1) **(2014)** 1-8.

42. Hutchison I., Chua M. S., . Browne H. L., Trapani V., Bradshw T. D., Westwell A. D. *J. Med. Chem*, 6 **(2001)** 699.

(M.S. PATEL)

Signature of the Candidate

(Prof. K.C. PATEL)

Signature of the Supervising Teacher